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Invited/Research note

Monitoring congestive heart failure by multi-vector cardiac impedance from implanted devices

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Abstract Introduction: For monitoring pulmonary edema secondary to Congestive Heart Failure (CHF), we investigated trends of impedance between implanted electrodes. Methods: ICDs were implanted in 16 dogs and 5 sheep. Right ventricles were paced (230–250 bpm) for several weeks. Impedance was measured every hour along 4 intrathoracic, 2 intracardiac and 4 cardiogenic vectors. Cardiac function was assessed biweekly by catheterization and echocardiography. Left Atrial Pressure (LAP) was measured daily by an implanted sensor. Results: All animals developed CHF after 2–4 weeks of pacing (EF, 52 vs. 34%; LVEDV, 65 vs. 97 ml; LVEDP, 7 vs. 16 mm Hg; LAV, 17 vs. 33 ml; LAP, 7 vs. 26 mm Hg). Impedance decreased during CHF: LV-Can, 17 ± 9%; LV–RV, 15 ± 8%; LV–RA, 13 ± 6%; RV-Can, 13 ± 8%; RV_{coil}-Can, 8 ± 6%; RA-Can, 6 ± 6%. The LV-Can decrease was greatest and correlated well with LAP ($r^2 = 0.73$). All impedances were associated with circadian variability at the baseline, which diminished during CHF (5 ± 2% vs. 2 ± 1%). In CHF, cardiogenic impedances displayed reduced peak-to-peak amplitude and increased fractionation. Conclusions: As impedance decreased during CHF, left-heart trends were better correlated with LAP. Left-heart vectors may improve the detection of CHF compared to sensing by right-heart leads alone. This approach has important clinical implications for managing HF patients in ambulatory settings.

1. Introduction

Congestive heart failure is an imbalance in pump function, in which the heart fails to maintain the circulation of blood adequately. The most severe manifestation of CHF, Pulmonary Edema (PE), develops when this imbalance causes an increase in lung fluid secondary to leakage from pulmonary capillaries into the interstitium and alveoli of the lung. Heart failure can be subdivided into systolic and diastolic dysfunction. Systolic dysfunction is characterized by a dilated Left Ventricle (LV) with impaired contractility, while diastolic dysfunction occurs in a normal or intact left ventricle with impaired ability to relax and receive, as well as eject, blood. In the United States and other developed countries, heart failure is one of the most costly diseases in healthcare budgets, with 70% of expenses going to the treatment of acute heart failure decompensation [1–3]. Regular monitoring of heart failure patients, recommended in management programs, has not shown a conclusive impact on heart failure morbidity. Severe symptoms that typically lead to hospitalization occur late in the HF evolution cycle [3]. For example, PE or associated symptoms, such as dyspnea, was observed only at an average of 3 days prior to the hospital visit. Therefore, a reliable means of HF status monitoring is needed to detect early decompensation and ideally to prevent patient's hospitalization. Intrathoracic impedance, utilizing a Right Ventricular (RV) lead, has been shown to be a useful sensor for monitoring PE secondary to CHF [4–7]. The dilation of heart chambers (e.g. LA, RV or LV) or the accumulation of fluid during pulmonary congestion will form a better conductance, causing a corresponding decrease in intracardiac

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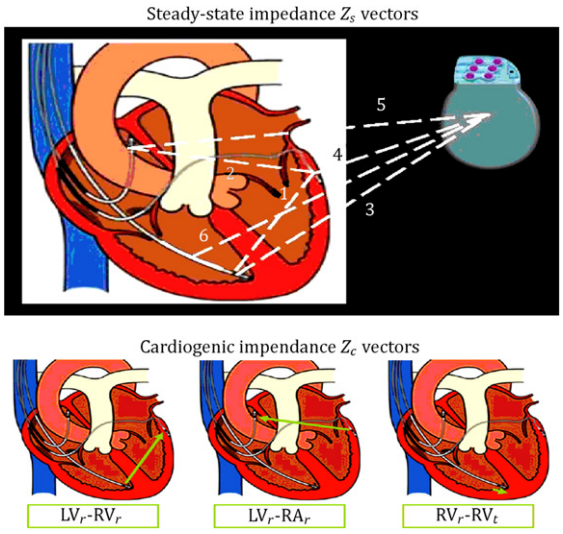

Figure 1: Vectors used to monitor Z_s and Z_c.

or intrathoracic impedance. In an attempt to understand how to improve the detection of CHF onset, we investigated trends in impedance measured between multiple implanted electrodes in an experimental model of induced heart failure.

2. Methods

Biventricular ICDs were implanted in two animal models: 16 dogs and 5 sheep. Standard transvenous leads were used, with the ICD-Can placed in the left pectoral region. Continuous RV pacing (230–250 bpm) was applied over several weeks. The ICD delivered, between pairs of electrodes, a train of current charge-and voltage-balanced multiphasic pulses (amplitude 0.5–1 mA; frequency 16 kHz), and measured the corresponding voltage. Steady-state impedance was determined as the ratio between measured voltage and injected current. Multiple signals were measured through the ring (r), the coil (c) and the device Can electrodes. The ICD device sampled the steady-state impedance (Z_s) every hour, and daily averages were computed. All measurements were made while pacing was temporarily halted. Stored data were automatically transferred through wireless communication. As illustrated in Figure 1, Z_s was measured every hour along 2 intracardiac vectors: RV_{ring}–LV_{ring} (1 — RV–LV) and LV_{ring}–RA_{ring} (2 — LV–RA) and 4 intrathoracic: RV_{ring}-Case(3 — RV-Can), LV_{ring}-Can(4 — LV-Can), RA_{ring}-Case(5 — RA-Can) and RV_{coil}-Can(6 — RV_c-Can). Continuous cardiogenic impedance (Z_c) signals were recorded and delivered over 3 bipolar (LV_{ring}–RA_{ring} (V1), RV_{ring}–LV_{ring} (V2) and RV_{ring}–RV_{tip} (V3)) and 1 quadripolar (RV–LV (V4)) vector configurations.

Cardiogenic impedance represented the instantaneous beat-to-beat changes in impedance, as caused by the mechanical contractions of the heart. Constant currents were injected and voltages measured from the electrode configurations above. All signals were sampled at 128 Hz. Daily averages were trended. The circadian variability, defined as the difference between the maximum Z_s and the minimum Z_s, between 0:00 and 23:59 on each day, was also monitored. In dogs, LV End-Diastolic Volume (LVEDV), LV Ejection Fraction (LVEF), LV End-Diastolic Pressure (LVEDP) and Left Atrial (LA) volume were measured every 2 weeks. In $N = 10$ animals, Left-Atrial Pressure (LAP) was measured daily, using an implantable IC sensor (HeartPOD - St. Jude Medical). Figure 1 shows the Z_c vectors and Figure 2 provides details about the LAP sensor.

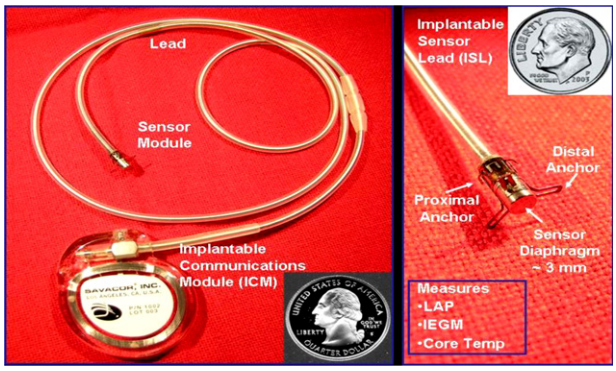

Figure 2: Implantable left-atrial pressure sensor.

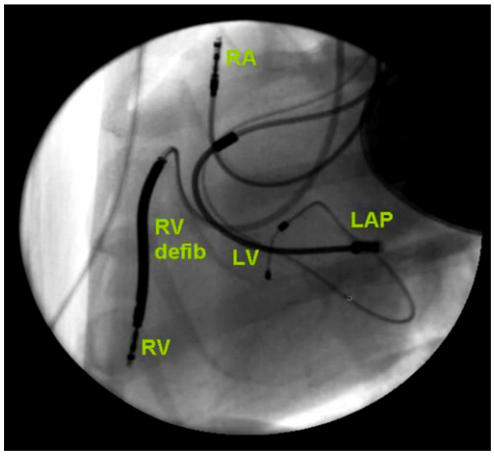

Figure 3: Fluoroscopic image of RA, RV and LV leads along with LAP sensor.

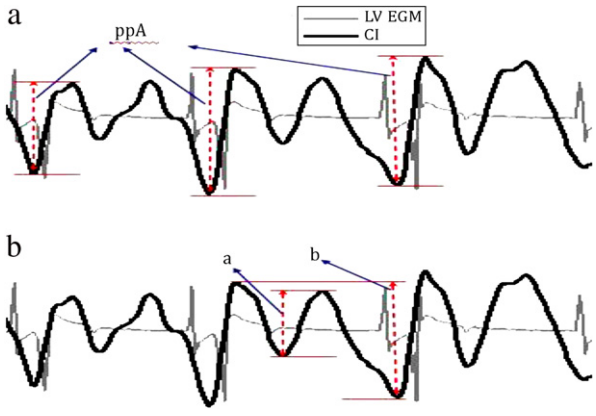

Figure 4: Peak-to-peak and fractionation index for Z_c.

Figure 3 illustrates a typical placement of leads (including the LAP lead) inside an animal's thorax.

Cardiogenic impedance data were analyzed by processing the peak-to-peak (ppA) amplitude of the signal and by assessing the Fractionation Index (FI). If a notch was present on a slope, FI was defined as the size of the notch, divided by the amplitude of peak. As presented in Figure 4, for each cardiac cycle, FI $= a/b$.

Table 1: Circadian variability in impedance.

Vector	ΔZ baseline[a] (Ω)	$\Delta\%Z$ baseline[b] (%)	ΔZ HF (Ω)	$\Delta\%Z$ HF (%)	% change in ΔZ from baseline to HF
RVc-Case	5.38	9.13	1.42	2.63	73.60[c]
LVr-RAr	24.3	4.02	12.8	2.40	47.40[c]
RVr-LVr	16.0	2.95	7.19	1.52	55.04[c]
LVr-Case	15.7	4.14	9.13	2.83	41.87[c]
RAr-Case	19.8	6.15	7.79	2.60	60.72[c]
RVr-Case	10.1	3.79	3.96	1.71	60.60[c]

[a] ΔZ: Change in Z from daytime to nighttime in Ω.
[b] $\Delta\%Z$: Percent change in Z from daytime to nighttime.
[c] $p < 0.05$.

Table 2: Trends in cardiogenic impedance during HF.

Vector	ppA healthy (Ω)	ppA HF (Ω)	ppA % change	FI healthy	FI HF	FI – % responder rate	LAP correlation coefficient
LVr-RAr	22.5	14.4	−34.4	0.17	0.43	100	−0.31
RV–LV Quad	1.87	1.01	−45.9	0.25	0.37	80	−0.75
RVr-LVr	28.1	17.0	−41.4	0.23	0.32	50	−0.68
RVr-RVt	45.9	15.7	−68.3	0.086	0.17	60	−0.76

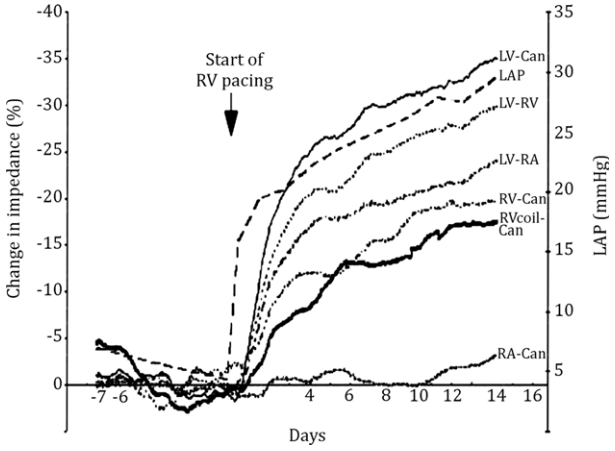

Figure 5: Changes in Z_s trend inversely with LAP.

3. Results

All animals developed CHF after 2–4 weeks of pacing from baseline, as evidenced by deterioration in function and hemodynamics (LVEF, 52 vs. 34%; LVEDV, 65 vs. 97 ml; LVEDP, 7 vs. 16 mm Hg; LAV, 17 vs. 33 ml; LAP, 7 vs. 26 mm Hg), clinical symptoms or autopsy. All impedance vectors decreased during CHF: LV-Can, 17% ± 9%; RV–LV, 15% ± 8%; LV–RA, 12% ± 6%; RV-Can, 12% ± 8%; RV_c-Can, 8% ± 6%; and RA-Can, 5% ± 6%. Typical Z_s impedance trends showed an increase during the first 30 days after implant, as leads matured. The Z_s impedance then decreased according to percentages above, as the animal was rapidly paced into HF. Animals typically recovered within 1–2 weeks after cessation of rapid pacing and Z_s impedance increased back to their baseline values. When animals were administered diuretics (i.e. fulosemide), the intake had the effect of significantly reducing the animal's fluid content and as a result of significantly increasing Z_s of all six vectors.

The addition of an LV lead improved impedance sensitivity to CHF with LV-Can highly sensitive compared to vectors based on RV-Can, RV_c-Can or RA-Can alone ($P < 0.05$). Z changes in RV–LV and LV–RA vectors were also significant as compared to RV_c-Can or RA-Can ($P < 0.05$). In a linear regression model, the impedance of the LV-Can vector correlated well with LAP trends ($r^2 = 0.73 \pm 0.12$, $N = 10$), while RV-Can and RV_c-Can Z_s were less correlated ($r^2 = 0.43 \pm 0.22$ and $r^2 = 0.52 \pm 0.15$, respectively). The impedance of all vectors inversely trended with left-atrial pressure. At the initiation of rapid pacing, the LAP increased, followed by a gradual decrease in Z_s impedances. On average, the impedance lagged the LAP increase by 0.5–2 days. As shown in Figure 5, the change in the impedance of left-side vectors tracked best the LAP trend. For ease of comparison, note that Figure 5 shows the change in impedance with an inverted sign. A different animal study has shown that during animal recovery, the vector impedance trended back up to the close vicinity of its original value [5]. On average, the recovery in impedance occurred over an approximately 14-day period, with most of it taking place in the first 4 days [5]. The correlation to LAP was preserved during recovery [5]. The initial step in LAP may have been the result of our artificial HF model. As with most animal models, this model is not a perfect replica of clinical HF.

In all Z_s vectors with statistical significance, the impedance was lowest between midnight and 3 AM and highest between noon and 3 PM. The circadian variability decreased with worsening heart failure.

Table 1 summarizes the circadian variability results. The circadian variation was computed as the difference between the maximum and minimum of the monitored parameter during any particular day. The relative values were computed with respect to the base value of the monitored parameter. The table reflects the means for all animals. A visible morphology change in Z_c occurred within 1–2 days of pacing, progressing throughout HF induction, as quantified by ppA reduction and FI increase in all vectors. There was a significant ($p < 0.05$) inverse correlation between LAP and ppA in Z_c vectors. Table 2 summarizes daily average changes in ppA and FI with HF onset. The changes were referred to the initial values prior to pacing. The direction of changes was consistent as LAP increased. No post-pacing data were included.

A significant decrease in ppA and increase in FI occurred with the onset of HF. Percent responder rate indicates the percentage of animals whose FI increased with HF onset for a given vector. Inverse correlation between ppA and LAP was observed in all vectors, as demonstrated by negative correlation coefficients. Figure 6 shows a representative example of reduction in ppA and the appearance of fractionation notches with worsening HF.

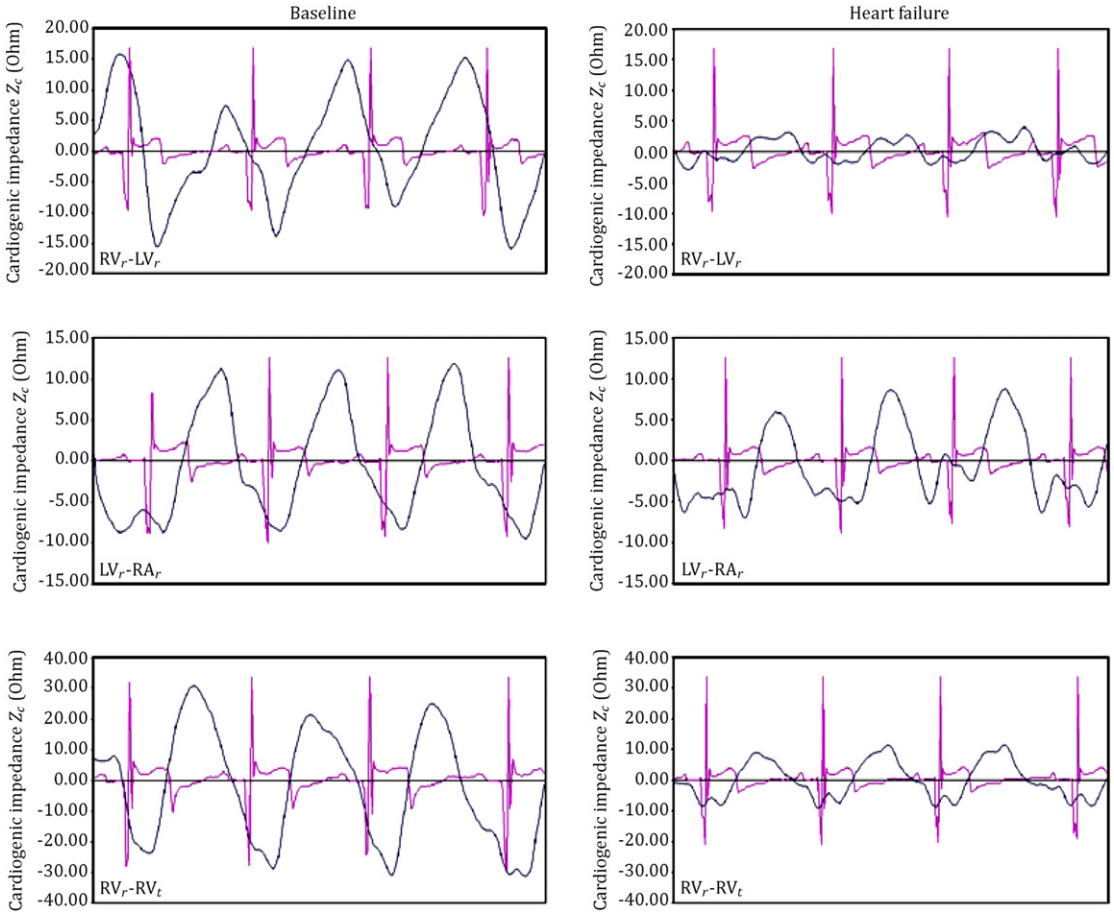

Figure 6: Variations in Z_c observed during progression from baseline to CHF, as evidenced by reduction in ppA and increase in FI of signals. The left-ventricular electrogram is displayed along with Z_c.

4. Conclusions

We observed a marked decrease in the impedance in all vectors after CHF onset. The addition of left-side vectors improved Z sensitivity and correlated well with LAP trends. Diuretics had an immediate effect, by increasing the impedance of all vectors. High variability between daytime and nighttime impedance was found, significantly decreasing with onset of HF. Due to animal model limitations, it was not evident whether the decrease in the circadian variability of impedance was linked to HF progression or to regularized RP heart rate. Onset of HF caused a significant decrease in ppA and an increase in FI in all cardiogenic impedance vectors, in all animals. A statistically significant inverse correlation between ppA and LAP was observed in three cardiogenic impedance vectors. The use of impedance for monitoring heart failure deserves further investigation. It is important to note that some of these results may not be reflective of clinical and human use of this technology. Our particular model of inducing heart failure by rapid RV pacing may have certain limitations.

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